

additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-1868.

In the Claims

Please cancel claims 74, 75, and 79.

Remarks

Claims 3, 57-73, 76-78, and 86 are pending and should be allowed upon entry of the accompanying Terminal Disclaimers. Claims 74, 75, and 79 have been canceled to facilitate prosecution. For purposes of clarification, it should be noted that claim 57(a), "providing a plurality of mutant microorganisms wherein each microorganism contains a different marker sequence", is NOT to be misconstrued as meaning "each *individual* microorganism harbors a different marker sequence". One of ordinary skill in the art will readily appreciate that the microorganisms are mutant because of a *heritable* change(s) in their DNA. Therefore, the genotype of a mutant may be propagated and passed on to daughter cells that are also present in the "plurality of mutant microorganisms".

Rejections Under 35 U.S.C. § 102

Claims 75 and 79 were rejected under 35 U.S.C. § 102(b) as being anticipated by Molecular Microbiology, Vol. 2, No.6, pages 757-766, by Finlay *et al.* ("Finlay"). Claims 74, 75, and 79 were rejected under U.S.C. § 102(b) as being anticipated by Journal of Bacteriology, Vol. 172, No. 7, pages 3738-3744 by Camilli *et al.* ("Camilli").

Claims 74, 75, and 79 have been canceled.

Double Patenting Rejections

Claims 3, 57-79 and 86 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-6, 8, 9, 12-22, and 24-31 of U.S. Patent No. 5,876,931. Claims 3, 57-79 and 86 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-21, and 25-26 of U.S. Patent No. 6,015,669. Claims 3, 57-60, 64-68, 71, 72, 74-79, and 86 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 10-15, and 21 of U.S. Patent No. 6,342,215.

In response, the applicant submits with this response:

- (1) a terminal disclaimer (petitioners, Imperial College Innovations Limited, owner of a joint and undivided interest in U.S. Patent No. 5,876,931; and Microscience Limited, owner of a joint and undivided interest in U.S. Patent No. 5,876,931) in compliance with 37 C.F.R. 1.321(c), certificates under 37 C.F.R. 3.73(b) and the appropriate fee for filing the terminal disclaimer;
- (2) a terminal disclaimer (petitioners, Imperial College Innovations Limited, owner of a joint and undivided interest in U.S. Patent No. 6,015,669; and Microscience Limited, owner of a joint and undivided interest in U.S. Patent No. 6,015,669) in compliance with 37 C.F.R. 1.321(c), certificates under 37 C.F.R. 3.73(b) and the appropriate fee for filing the terminal disclaimer; and
- (3) a terminal disclaimer (petitioners, Imperial College Innovations Limited, owner of a joint and undivided interest in U.S. Patent No. 6,342,215; and Microscience Limited, owner of a joint and undivided interest in U.S. Patent No. 6,342,215) in compliance with 37 C.F.R. 1.321(c),

U.S.S.N. 09/714,602

Filed: November 16, 2000

AMENDMENT AND RESPONSE TO OFFICE ACTION

certificates under 37 C.F.R. 3.73(b) and the appropriate fee for filing the terminal disclaimer. It should be noted that submission of the Terminal Disclaimers does not constitute an admission that applicants agree with this rejection but submit Terminal Disclaimers solely to facilitate prosecution.

Allowance of claims 3, 57-73, 76-78, and 86 is respectfully solicited.

Respectfully submitted,

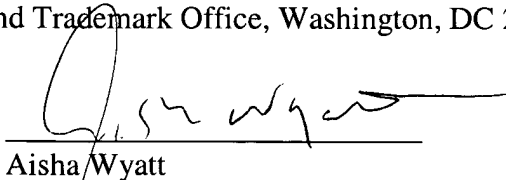


Patrea L. Pabst
Reg. No. 31,284

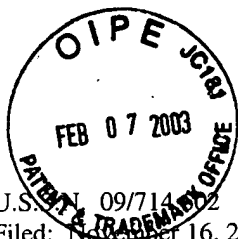
Date: February 3, 2003
HOLLAND & KNIGHT LLP
One Atlantic Center, Suite 2000
1201 West Peachtree Street
Atlanta, Georgia 30309-3400
(404) 817-8473
(404) 817-8588 (Fax)

Certificate of Mailing Under 37 C.F.R. § 1.8(a)

I hereby certify that this Amendment and Response to Office Action, and any documents referred to as attached or enclosed, is being deposited with the United States Postal Service on this date, February 3, 2003, with sufficient postage as first-class mail in an envelope addressed to the Commissioner for Patents, U.S. Patent and Trademark Office, Washington, DC 20231.


Aisha Wyatt

Date: February 3, 2003



U.S. PAT. 09/714,072
Filed: November 16, 2000

MARKED UP VERSION OF AMENDMENTS PURSUANT TO 37 C.F.R. § 1.121

Marked Up Version of Amended Claims

Pursuant to 37 C.F.R. § 1.121(c)(1)(ii)

3. (Amended) The method according to Claim 57 further comprising after step (a), removing auxotrophs from the plurality of mutant microorganisms.

57. A method for identifying a mutant microorganism having a reduced adaptation to a particular environment comprising the steps of

(a) providing a plurality of mutant microorganisms wherein each microorganism contains a different marker sequence;

(b) introducing the plurality of mutants of step (a) into the said particular environment and allowing those microorganisms which are able to do so to grow in the said environment;

(c) retrieving microorganisms from the said environment or a selected part thereof; and

(d) selecting an individual mutant having a reduced capacity to proliferate in the particular environment by comparing any marker sequences in the nucleic acid present in the retrieved microorganisms in step (c) to the different marker sequences referred to in step (a).

58. The method of Claim 57 for identifying a gene which allows a microorganism to adapt to a particular environment further comprising the step:

(e) identifying the gene which is mutated in the individual mutant having a reduced capacity to proliferate in the particular environment.

59. The method of Claim 58 for isolating a gene which allows a microorganism to adapt to a particular environment further comprising the step:

(f) isolating from a wild-type microorganism the corresponding wild-type gene.

60. The method of Claim 59 wherein the particular environment is a differentiated multicellular organism.

61. The method of Claim 60 wherein the multicellular organism is a plant.

62. The method of Claim 61 wherein the microorganism is a bacterium pathogenic to plants.

63. The method of Claim 61 wherein the microorganism is a fungus pathogenic to plants.

64. The method of Claim 60 wherein the multicellular organism is a non-human animal.

65. The method of Claim 64 wherein the animal is selected from the group consisting of a mouse, rat, rabbit, dog and monkey.

66. The method of Claim 65 wherein the animal is a mouse.

67. The method of Claim 64 wherein the microorganisms is a fungus pathogenic to animals.

68. The method of Claim 67 wherein the fungus is selected from the group consisting of *Aspergillus* spp., *Cryptococcus neoformans* and *Histoplasma capsulatum*.

69. The method of Claim 64 wherein in step (b) the microorganisms are introduced orally, intravenously, intranasally, or intraperitoneally.

70. The method of Claim 69 wherein in step (c) the microorganisms are retrieved from the spleen.

71. The method of Claim 64 wherein the microorganism is a bacterium pathogenic to animals.

72. The method of Claim 71 wherein the bacterium is selected from the group consisting of *Bordetella pertussis*, *Campylobacter jejuni*, *Clostridium botulinum*, *Escherichia coli*, *Haemophilus decreyi*, *Haemophilus influenzae*, *Helicobacter pylori*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria* spp., *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pseudomonas* spp., *Salmonella* spp., *Shigella* spp., *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Vibrio* spp., and *Yersinia pestis*.

73. The method of Claim 60 wherein in step (c) the microorganisms are retrieved from the said environment at a site remote from the site of introduction in step (b).

Please cancel claims 74 and 75

76. The method of Claim 57 wherein the microorganism is a bacterium.

77. The method of Claim 57 wherein the microorganism is a fungus.

78. The method of Claim 57 wherein in step (d) the comparison of any marker sequences in the nucleic acid of the mutants retrieved in step (c) to the marker sequences referred to in step (a) uses DNA amplification techniques and oligonucleotide primers.

Please cancel claim 79.

80. A non-human animal or plant, or an animal or plant cell culture, containing a plurality of mutant microorganisms wherein each mutant contains a different marker sequence.

81. The non-human animal or plant, or an animal or plant cell culture, of Claim 80 wherein the microorganism is a pathogenic microorganism.

82. A non-human animal or an animal cell culture containing a plurality of mutant microorganisms wherein each mutant contains a different marker sequence and wherein the microorganism is pathogenic to animals.

83. The non-human animal or an animal cell culture of Claim 82 wherein the microorganism is selected from the group consisting of *Bordetella pertussis*, *Campylobacter jejuni*, *Clostridium botulinum*, *Escherichia coli*, *Haemophilus ducreyi*, *Haemophilus influenzae*, *Helicobacter pylori*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria* spp., *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pseudomonas* spp., *Salmonella* spp., *Shigella* spp., *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Vibrio* spp., and *Yersinia pestis*.

84. The non-human animal of Claim 83 which is a mouse or rat or rabbit or dog or monkey.

85. The non-human animal of Claim 82 which is a mouse or rat or rabbit or dog or monkey.

86. A method for identifying a microorganism having a reduced adaptation to a particular environment comprising the steps of

(a) providing a plurality of microorganisms wherein each microorganism contains a different marker sequence;

(b) introducing the plurality of microorganisms of step (a) into the said particular environment and allowing those microorganisms which are able to do so to grow in the said environment;

(c) retrieving microorganisms from the said environment or a selected part thereof; and

(d) selecting an individual microorganism having a reduced capacity to proliferate in the particular environment by comparing any marker sequences in the nucleic acid present in the retrieved microorganisms in step (c) to the different marker sequences referred to in step (a).